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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,565	04/07/2004	I. Ross Garrett	432722003700	8570

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EXAMINER	
WEDDINGTON, KEVIN E	

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1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,565	GARRETT ET AL.	
	Examiner	Art Unit	
	Kevin E. Weddington	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-45* is/are rejected.

7)☒ Claim(s) *46 and 47* is/are ~~objected to~~. will not be examined as stated in the Office action.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-14-04; 12-21-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-47 are presented for examination.

Applicants' drawings filed April 7, 2004 and the information disclosure statements filed October 14, 2004 and December 21, 2004 have been received and entered.

Applicants' election filed May 24, 2007 in response to the restriction requirement of February 27, 2007 has been received and entered. The applicants elected the invention described in claims 40-47 (Group II) without traverse. The applicants also elected: a) statin is cerivastatin; b) NO is L-arginine; and d) the elected combination of claim 45, (at least one nitric oxide generating system and at least one statin-like compound).

Claims 1-39 are withdrawn from consideration as being drawn to the non-elected invention (37 CFR 1.142(b)).

Claims 46 and 47 will not be examined because they contain non-elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection.

Claims 40-45 described compounds that are nitric oxide generating system, statin-like compound, and phosphodiesterase inhibitor. The instant claims cover all compounds having the pharmaceutical property of being a nitric oxide generating system, a statin-like compound to enhance bone formation. Describing a compound by its functions will not substitute for written description of the structure of the compound. The invention should be described in such a way as to described what the invention is, not what the invention does. Describing the function of a compound fails to distinguish the compound from other molecules or agents that can perform the same functions.

Undue experimentation is a conclusion reaches by weighing the noted factual considerations set forth below as seen in In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1401 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors include:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice that instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

Claims 40-45 are directed to compounds that are nitric oxide generating system, statin-like compound, and phosphodiesterase inhibitor that are used to enhance bone formation. The instant claims cover all compounds having pharmaceutical property of being known as a compound (nitric oxide generating system, statin-like compound, and phosphodiesterase inhibitor) to enhance bone formation. Although claims 41, 43 and 44 lists specific examples of compounds which are alleged to have the property to enhance bone formation, and claims 40, 42 and 45 are directed to a variety of compounds with the functional description of being known as a compound which is alleged to have the property to enhance bone formation.

The instant claims are very broad. For instance, claims 40, 42 and 45 are to a plethora of compounds of as described by the functional properties as being known to enhance bone formation.

The relative skill of those in the art is generally that of a Ph.D. or M.D.

One skilled in the art would not predict from the instant disclosure which compounds would fall under the umbrella of functional description of being known as broadly as nitric oxide generating system, statin-like compound, and phosphodiesterase inhibitor. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances.

The breadth of the claims

The claims are very broad and inclusive to all nitric oxide generating system, statin-like compound, and phosphodiesterase inhibitor that are used to enhance bone formation.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples only show the combination of statin-like compound, simvastatin, combined with L-arginine.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to how the skilled artisan would be able to extrapolate from the disclosure and examples provided to make and

possibly use the claimed invention. The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. (In re Fischer, 427 F. 2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823).

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or of the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all the compounds or agents that are broadly known to possess the property of enhancing bone formation as described in this specification. In view of the information set forth supra, the instant disclosure is not seen to be sufficient to describe the use of any compound , which is regarded as the functional description of a compound (nitric oxide generating system, statin-like compound, and phosphodiesterase inhibitor) for enhancing bone formation.

Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

Claims 40-45 are not allowed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 40-43 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaesemeyer (5,968,983) of PTO-1449.

Kaesemeyer teaches a therapeutic mixture (composition) comprising an inhibitor of Hmg-CoA reductase (a statin-like compound), and a substrate of NOS (a biological equivalent of arginine). Note column 11, claims 13 and 15 discloses the statin-like compounds; and column 11, claim 16 discloses L-arginine.

Note that a composition comprising the same ingredients as the claimed composition will inherently possess the qualities recited herein. Note further that recitation of intended use does not further limit a claim drawn to a composition.

Claims 40-43 and 45 are not allowed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be

> patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 40-43 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vogel, "Cholesterol-Lowering Drugs May Boost Bones", Science, Vol. 286, No. 5446, pp. 1825-1826 (Dec. 1999) or Garrett et al., "Statins and Bone Formation", Current Pharmaceutical Design, Vol. 7, No. 8, pp.715-736 (May 2001) in view of Visser et al., "Arginine supplementation in the prevention and treatment of osteoporosis", Medical Hypotheses, Vol. 43, No. 5, pp. 339-342 (Nov. 1994).

Vogel teaches cholesterol-lowering drugs such as statins can be able to increase bone growth in patients with osteoporosis (see the abstract).

Garrett et al. teach statins are capable of increasing bone formation and bone mass in rodents suggests a potential new action for the statins (see the abstract).

The instant invention differs from the cited references in that the cited references do not teach the addition of a NO donor such as L-arginine. However, the secondary reference, Vesser et al., teaches L-arginine in pharmacological doses potentially increase bone formation over bone resorption, and consequently, increase bone mass (see the abstract).

Clearly, one skilled in the art would have assumed the combination of two individual agents well-known to promote bone growth into a single composition will give an additive effect in the absence of evidence to the contrary.

Claims 40-43 and 45 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin E. Weddington whose telephone number is (571)272-0587. The examiner can normally be reached on 12:30 pm-9:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kevin E. Weddington
Primary Examiner
Art Unit 1614

K. Weddington
June 10, 2007